TOBACCO-SPECIFIC AND VOLATILE N-NITROSAMINES IN ENVIRONMENTAL TOBACCO SMOKE

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ABSTRACT

N-Nitrosonornicotine (NNN) and 4-(N-methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), two tobacco-specific N-nitrosamines (TSNA), as well as the volatile N-nitrosamines N-nitrosodimethylamine (NDMA) and N-nitrosopyrrolidine (NPYR) were determined in the indoor air of a poorly ventilated office and in real-life situations where extensive smoking occurred. Smoking in the office resulted in indoor air concentrations of 7.6-20.0 ppm carbon monoxide (CO) and 58.5-132 μg/m³ nicotine. The mean nitrosamine concentrations (in ng/m³) were: 2.8 [not detected (nd)-6.0] NNN, 4.9 (nd-13.5) NNK, 19.8 (7.9-45.0) NDMA and 10.0 (3.5-27.0) NPYR. Under real-life conditions, indoor air contained 0.8-2.1 ppm CO and 8.5-45.8 μg/m³ nicotine. Nitrosamine concentrations (ng/m³) were nd-2.0 NNN, nd-2.3 NDMA and traces of NPYR (limit of detection 0.3 ng/m³). NNK was not found. Exposure of a nonsmoker under normal real-life conditions to <0.005 μg TSNA and volatile N-nitrosamines over 3 h provides only a very small contribution to the total daily N-nitrosamine exposure of 10-100 μg/day.

INTRODUCTION

Tobacco-specific N-nitrosamines (TSNA) such as N-nitrosonornicotine (NNN), N-nitrosoanatabine, N-nitrosoanabasine and 4-(N-methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) are found in cured tobacco and transfer to mainstream and sidestream smoke during smoking (1,2). As a result, trace quantities of TSNA could be present in environmental tobacco smoke (ETS). In two studies we have determined indoor air concentrations of NNN and NNK, as well as the presence of the volatile N-nitrosamines N-nitrosodimethylamine (NDMA) and N-nitrosopyrrolidine (NPYR). Both NDMA and NPYR occur ubiquitously in the environment (3) and are not specific to tobacco smoke. In both studies nicotine was determined as a surrogate marker for ETS and carbon monoxide (CO) as a marker of indoor air quality. The first study was performed in a poorly ventilated ground floor office in Vienna in which extensive smoking occurred. In the second study additional tobacco-specific components (solanesol, 3-ethenylpyridine) and respirable suspended particles (RSP) were determined under real-life conditions in two restaurants, two smoking compartments in a train, and in the home of a smoker.

MATERIALS AND METHODS

The ground floor office (84 m³) was not air-conditioned and was furnished with standard office fittings. Indoor air was sampled for 2 h on 14 different occasions, during which the office was occupied by up to 5 people (smokers and nonsmokers). No attempt was made to

influence the smoking habits and working activity of the occupants, who were free to leave and enter the office at any time. However, it was not permitted to open the windows during the air monitoring sessions. The number of people present, as well as the times when cigarettes, cigars and pipes were lighted, were recorded. The sampling apparatus was located close to the center of the office and installed at the breathing height of a seated person. Nicotine, volatile N-nitrosamines and TSNA were determined according to a published methods (4,5). The presence of N-nitrosamines was confirmed by rechromatography after photolysis of the sample at 365 nm (6). Direct on-line measurement was performed for CO (Carbon Monoxide Analyzer Model 8310; Monitor Labs Inc., USA) and nitrogen oxides (Nitrogen Oxide Analyzer Model 8840; Monitor Labs Inc., USA).

Indoor air monitoring under real-life conditions was performed unobstrusively using a modified portable air sampling system (Portable Air Sampler, TNO, Division of Technology, Delft, The Netherlands (7)). A time-weighted air sample was collected using a Tedlar (PVF) sampling bag for analysis of CO by direct on-line measurement as discribed above. Nicotine (8), 3-ethenylpyridine (9), RSP (10) and solanesol (11) were determined according to published methods. A self-constructed portable air sampling case was used for collection of volatile N-nitrosamines and TSNA on Extrelut columns (E. Merck; Darmstadt, Germany) saturated with aqueous phosphate/citrate buffer (pH 3.5) containing 10 % glycerin and ascorbic acid to inhibit artifact formation of N-nitrosamines. After sampling, the column was extracted with methylene chloride and the extract analyzed as previously published (4).

RESULTS

The time-integrated office air concentrations of tobacco smoke constituents together with the amount of tobacco burned in the office are shown in Table 1. On average, 0.075 g/h/m^3 of tobacco (range 0.52-0.104 g/h/m^3) was smoked during the 14 sessions. The following approximate tobacco weights were assumed: 0.8 g for cigarette tobacco; 1.2 g for pipe tobacco and 7 g for cigar tobacco. As a surrogate marker of ETS, the mean nicotine concentration was 90.1 µg/m^3 (range 58.5-132 µg/m^3). Mean concentrations of CO and nitrogen oxides (NOx) were 11.5 ppm (7.6-20.0 ppm) and 158 ppb (109-290 ppb), respectively. The mean nitrosamine concentrations (in ng/m^3) were: 2.8 [not detected (nd)-6.0] NNN, 4.9 (nd-13.5) NNK, 19.8 (7.9-45.0) NDMA and 10.0 (3.5-27.0) NPYR.

Time-integrated real-life concentrations of RSP and tobacco smoke components are presented in Table 2. The nicotine and CO concentration ranged between 8.5-45.8 µg/m^3 and 0.8-2.1 ppm, respectively. Mean nitrosamine concentrations (in ng/m^3) ranged from nd-2.0 NNN, nd-2.3 NDMA and traces of NPYR. NNK was not detected subject to a detection limit of 0.3 ng/m^3 for a 3 h sampling period. NOx were not determined under real-life conditions since it was not possible to perform unobstrusive direct on-line measurements.

DISCUSSION

Under the semi-controlled conditions in which time-integrated office air concentrations of tobacco smoke components were measured in a poorly ventilated office in which extensive smoking took place, no correlation was observed between the amount of tobacco burnt (range 0.052-0.104 g/h/m^3) and individual components of ETS. This may be due to differences in the types of tobacco products smoked on the various occasions and ventilation conditions in the office. Subjects (both smokers and nonsmokers) present in the office during air sampling complained about the bad air conditions (7.6-20.0 ppm CO). This allows the conclusion that,

normally, the air quality would have been improved by opening the windows. This is further confirmed by the nicotine concentrations in the indoor air which ranged between 58.5 and 132 $\mu g/m^3$ (mean 90.1 $\mu g/m^3$) which are considerably higher than reported concentrations of <50 $\mu g/m^3$, most frequently <20 $\mu g/m^3$, in offices with unrestricted ventilation (12-15). Poor ventilation conditions resulted in ETS concentrations of 5-15 ng/m^3 NNN and NNK.

Table 1. Time-integrated ETS constituents in an office with restricted ventilation.

Tobacco burnt ($g/h/m^3$) [product][1]	Nicotine ($\mu g/m^3$)	CO (ppm)	NOx (ppb)	Nitrosamine concentrations (ng/m^3) NNN	NNK	NDMA	NPYR
0.059 [11c,1Z]	132.0	12.5	110	1.7	0	27.2	11.6
0.086 [18c]	27.0	13.0	157	0	1.6	13.2	4.9
0.099 [12c,1p]	117.6	12.4	182	3.1	3.1	13.9	5.9
0.082 [7c,1p,1Z]	101.7	11.4	133	2.9	4.7	23.0	8.0
0.104 [13c,1p]	100.4	11.0	140	4.9	2.1	7.9	5.2
0.075 [7c,1p]	93.7	9.0	194	6.0	4.2	14.0	27.0
0.052 [11c]	89.8	7.7	109	1.6	4.4	22.0	13.0
0.080 [8c,1p]	87.8	20.0	290	2.6	8.0	25.2	10.3
0.071 [15c]	84.1	14.0	192	3.8	10.8	9.0	4.5
0.070 [6c,1p]	72.3	8.7	110	2.3	4.9	36.0	11.0
0.052 [11c]	69.8	7.6	125	3.5	13.5	8.2	3.5
0.052 [11c]	64.2	10.4	120	1.4	2.8	12.8	6.8
0.089 [10c,1p]	61.9	13.0	172	3.8	4.5	na[2]	na
0.075 [7c,1p]	58.5	10.7	175	1.6	3.3	45.0	18.1

[1]Tobacco burnt = 0.8 g/cigarette [c]; 1.2 g/pipe [p]; and 7.0 g/cigar [Z].
[2]na = not analyzed.

Under real-life conditions during which even more extensive smoking occurred on two occasions (0.059-0.211 $g/h/m^3$ tobacco burnt), normal ventilation conditions greatly improved the air quality (0.8-2.1 ppm CO; 8.5-45.8 $\mu g/m^3$ nicotine) and lower concentrations of nd-2.0 ng/m^3 NNN, nd-2.3 ng/m^3 NDMA and traces of NPYR were detected. NNK was not found. The laboratory personel, all nonsmokers, who performed the sampling did not complain about the air quality on any sampling occasion.

The presence of NNN and NNK in ETS is solely due to tobacco smoke. However, volatile N-nitrosamines such as NDMA and NPYR occur ubiquitously in the environment (3), and concentrations as high as 10-90 ng/m^3 have been reported in ambient air of industrial areas (16). As a result, the presence of NDMA and NPYR in indoor air is not specifically due to ETS. The levels of TSNA reported in indoor air in Table 2 are considerably lower than those recently reported by Brunnemann et al. (17) who did not determine a surrogate marker for ETS. They only noted that CO was unsuitable as a marker for this purpose.

Under restricted ventilation conditions resulting in poor air quality, occupation of the office by a nonsmoker for 1 h would result in a maximum exposure of 0.01 $\mu g/h$ TSNA and 0.03

µg/h volatile N-nitrosamines. These exposure levels are based on the highest values shown in Table 1 and assuming a respiratory volume of 0.5 m^3/h with total retention of all N-nitrosamines. Despite the fact that smoking intensity on two occasions was higher under real-life conditions, lower concentrations of 8.5-45.5 µg/m^3 nicotine (mean 23.8 µg/m^3) were determined confirming that the poor ventilation conditions in the office contributed heavily towards elevations in indoor air concentrations of ETS components. Under real-life conditions (Table 2), nonsmoker exposure of <0.005 µg/h total N-nitrosamines occurs.

Table 2. Time-intergrated ETS constituents under real-life conditions.

	Restaurants		Train compartments		Smoker
	1	2	1	2	home
Room size (m^3)	100	800	65	65	75
Sampling time (min)	180	180	175	28	190
Tobacco products (c,p,z)[1]	32c	159c	20c	8c	12c,3z
Tobacco burnt (g/h/m^3)[2]	0.128	0.066	0.082	0.211	0.059
Particulate phase					
RSP (µg/m^3)	272.6	165.6	14.5	207.7	203.1
Solanesol (µg/m^3)	0.39	1.35	<0.02	<0.1	1.15
Gas phase					
CO (ppm)	2.1	1.1	0.8	na[3]	1.1
Nicotine (µg/m^3)	45.8	13.5	27.5	23.5	8.5
3-Ethenylpyridine (µg/m^3)	7.0	3.9	4.2	4.7	2.4
N-Nitrosamines					
NDMA (ng/m^3)	1.7	2.3	1.6	nd[4]	tr[5]
NPYR (ng/m^3)	tr	tr	tr	nd	tr
NNN (ng/m^3)	0.7	1.5	2.0	nd	nd
NNK (ng/m^3)	nd	nd	nd	nd	nd

[1]Tobacco products abbreviated as: c, cigarette; and z, cigarillo.
[2]Tobacco burnt = 0.8 g/cigarette and 1.5 g/cigarillo.
[3]na = not analyzed.
[4]nd = not detected (limit of detection 0.3 ng/m^3)
[5]tr = trace (<0.5 ng/m^3)

Assuming an ETS exposure of 3 h/day, which has been found as typical for ETS exposure under real-life conditions in Gennany (18), the daily exposure to N-nitrosamines from our studies on real-life ETS amounts to <0.005 µg combined TSNA and volatile N-nitros-amines. This is considerably smaller than the average daily dietary intake of 0.2-0.3 µg of volatile N-

nitrosamines (19), and an estimated total daily dietary intake of 10-100 µg for all N-nitrosamines (20). As a result, it is concluded that exposure to N-nitrosamines in ETS provides only an insignificant contribution to the exogenous total daily N-nitrosamine exposure, and is also negligible compared to the potential for endogenous nitrosamine formation from nitrosatable secondary amines (21). Nicotine, a tertiary amine, nitrosates only very slowly in vitro under aqueous conditions to form NNN, NNK and 4-(N-methyl-nitrosamino)-4-(3-pyridyl)-1-butanal (22) and no evidence exists to show that endogenous nitrosation of nicotine occurs (23).

REFERENCES

1. Hoffmann D, Adam JD, Brunnemann KD, Hecht SS. Assessment of tobacco-specific N-nitrosamines in tobacco products. Cancer Res 1979;39:2505-9.
2. Tricker AR, Ditrich C, Preussmann R. N-Nitroso compounds in cigarette tobacco and their occurrence in mainstream tobacco smoke. Carcinogenesis 1991;12:257-61.
3. Tricker AR, Spiegelhalder B, Preussmann R. Environmental exposure to preformed nitroso compounds. Cancer Surv 1989;8:251-72.
4. Klus H, Begutter H, Scherer G, Tricker AR, Adlkofer F. Tobacco-specific and volatile N-nitrosamines in environmental tobacco smoke of offices. Indoor Environ 1992;1:348-50.
5. Begutter H, Klus H, Ultsch L. Kapillargaschromatographische Bestimmung flüchtiger und tabakspezifischer N-Nitrosamine mittels des Thermo Energy Analyzers. J Chromatogr 1985;321:475-9.
6. Fiddler W, Doerr RC, Piotrowski EG. Observations on the use of thermal energy analyzer as a specific detector for nitrosamines. In: Walker EA, Castegnaro M, Griciute L, Lyle RE, ed., Environmental aspects of N-nitroso compounds, IARC Scientific Publications No. 19. Lyon: International Agency for Research on Cancer, 1978:33-9.
7. Van der Wal JF, Portable air sampler for measurements in aircraft and public buildings. In: Bieva CJ, Courtois Y, Govaerts M, eds. Present and future of indoor air quality. Amsterdam: Elsevier Science Publisher B.V., 1989:371-8.
8. Ogden ME. Gaschromatographic determination of nicotine in environmental tobacco smoke: Collaborative study. J Assoc Off Anal Chem 1989;72:1002-6.
9. Eatough DJ, Benner CL, Tang H, et al., The chemical composition of environmental tobacco smoke. III. Identification of conservative tracers of environmental tobacco smoke. Environ Int 1989;15:19-28.
10. Conner JM. Developement of a method for estimating the contribution of environmental tobacco smoke (ETS) to indoor air respirable suspended particles. Paper presented at the 40th Tobacco Chemists' Research Conference. October 13-16, 1986, Knoxville, Tenessee, USA.
11. Ogden MW, Maiolo K. Comparison of GC and LC for determining solanesol in environmental tobacco smoke. Paper presented at the 44th Tobacco Chemists' Research Conference, October 1-3, 1990, Winston-Salem, North Carolina, USA.
12. Muramatsu M, Umemura S, Okada T, Tomita H. Estimation of personal exposure to tobacco smoke with a newly developed nicotine personal monitor. Environ Res 1984;35:218-27.
13. Hammond SK, Leaderer BP, Roche AC, Schenker M. Collection and analysis of nicotine as a marker for environmental tobacco smoke. Atmos Environ 1987;21:457-62.

14. Proctor CJ, Warren ND, Bevan MAJ. Measurements of environmental tobacco smoke in an air conditioned office building. Environ Technol Lett 1989;10:1003-18.
15. Coultas DB, Samet JM, McCarthy JF, Spengler JD. A personal monitoring study to assess workplace exposure to environmental tobacco smoke. Am J Public Health 1990;80:988-90.
16. Akkan Z, Preussmann R, Spiegelhalder B. N-Nitrosamines in ambient air of indust-l areas in Germany. J Cancer Res Clin Oncol 1991;117:S14.
17. Brunnemann KD, Cox JE, Hoffmann D. Analysis of tobacco-specific N-nitrosamines in indoor air. Carcinogenesis 1992;13:2415-8.
18. Letzel HW, Johnson LC. The extent of passive smoking in the Federal Republic of Germany. Prev Med 1984;13:717-29.
19. Tricker AR, Pfundstein B, Theobald E, Preussmann R, Spiegelhalder B. Mean daily intake of volatile N-nitrosamines from foods and beverages in West Germany in 1989-1990. Food Chem Toxicol 1991;11:729-32.
20. Tricker AR, Preussmann R. Carcinogenic N-nitrosamines in the diet: Occurrence, formation, mechanisms and carcinogenic potential. Mutation Res 1991;259:277-89.
21. Tricker AR, Pfundstein B, Preussmann R. Nitrosatable secondary amines: exogenous and endogenous exposure, and nitrosation in vivo. In: Loeppky RN, Michejda C, eds. Nitrosamines and N-nitroso compounds. Washington DC: American Chemical Society Books, 1993:in press.
22. Caldwell WS, Greene JM, Plowchalk DR, deBethizy JD. The nitrosation of nicotine: A kinetic study. Chem Res Toxicol 1991;4:513-6.
23. Tricker AR, Scherer G, Conze C, Adlkofer F, Pachinger A, Klus H. Evaluation of 4-(N-methylnitrosamino)-4-(3-pyridyl)butyric acid as a potential monitor of endogenous nitrosation of nicotine and its metabolites. Carcinogenesis, submitted for publication.